REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1-12 were pending in this application when last examined.

Claims 1-4 and 9-11 have been examined on the merits and stand rejected.

Claims 5-8 and 12 are withdrawn as non-elected subject matter.

Claims 1, 4 and 9 have been amended.

Claim 1 has been amended to delineate and clarify the method steps. Support for these changes can be found in original claim 1.

Claim 1 has also been amended to clarify the components of the recombinant adenovirus vector. For instance, the recombinant cosmid/adenovirus vector in step (i) of claim 1 comprises an adenovirus genome DNA and a DNA sequence, wherein the DNA sequence is inserted into the adenovirus genome DNA at the deletion site of either the El region or the E1 and E3 regions of the adenovirus genome DNA. Support for these insertion sites can be found in original claim 9 and in Fig. 1. Also, support for the "DNA sequence of the cosmid sequence" and the "outer sequences" in step (i) of claim 1 and in claim 9 is apparent from the overall description in the specification, especially, at page 9, lines 17-20 and Figs. 1 and 3. The construct obtained in step (i) of claim 1 is exemplified in Figs. 1 and 3.

Support for the conclusion step (iii) of claim 1 can be found in the specification, for example, at page 15, line 28 to page 16, line 2 and in Figs. 1 and 3.

Support for the amendment to claim 4 to recite "cells" instead of "cell line" can be found in the specification, for example, at page 10, last line to page 11, line 5. As disclosed in the specification, the 293 cell line is only one preferred embodiment.

Claim 9 has been amended to clarify the structure (circular DNA construct) and components (a DNA sequence and an adenovirus genome DNA) of the cosmid/adenovirus vector. Support for

this amendment can be found in the specification, for example, at page 6, lines 16-20. See also page 4, lines 6-7, 26-27, page 9, lines 8-20, Figure 1, and the Abstract.

Therefore, no new matter has been added by this amendment.

II. OBJECTION TO THE CLAIMS

Claims 1, 4 and 9 were objected to for containing typographical/spelling errors. See the 5th -7th paragraphs on page 2 of the Office Action.

It is respectfully submitted that the present amendment overcomes this objection to the claims by correcting the errors noted in the Office Action.

Therefore, the objection to claims 1, 4 and 9 is untenable and should be withdrawn.

III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-4 and 9-11 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for the reasons set forth at page 3 of the Office Action.

Applicants respectfully traverse this rejection as applied to the amended for the following reasons.

Claim 1 has been amended to better clarify the components of the vector and to delineate the method steps in constructing the vector. Specifically, the recombinant cosmid/adenovirus vector in step (i) of claim 1 comprises an adenovirus genome DNA and a DNA sequence, wherein the DNA sequence is inserted into the adenovirus genome DNA at the deletion site of either the El region or the E1 and E3 regions. The claim also specifies that the DNA sequence consists of a cosmid sequence and outer sequences, wherein the cosmid sequence has recombinase recognition sequences at both ends thereof and the outer sequences arc extended from each of the recombinase recognition sequences. At least one of the outer sequences has a cloning site where the expression cassette is inserted into. This construct is exemplified in the attached copy Fig. 1 which has been marked-up to clarify the components.

The "outer sequences" are apparent from the disclosure on page 9, lines 17-20. The DNA sequence as an insert is apparent from the overall description, especially from Fig. 1.

Also, step (iii) of claim 1 now includes the conclusion step as described in the specification at page 15, line 28 to page 16, line 2, and in Figs. 1 and 3. Thus, from amended step (iii), it is clear that the recombinase acts to delete the cosmid sequence from the DNA sequence of the recombinant cosmid/adenovirus vector. As a result, the adenovirus genome DNA, a recombinase recognition site and the outer sequences of the DNA sequence remain in the construct. The expression cassette inserted into the outer sequence also remains. See Fig. 3A. Consequently, the resultant recombinant adenovirus vector comprises the adenovirus genome DNA and the expression cassette which has been inserted into the outer sequence.

Thus, the amendment to claim 1 overcomes the Examiner's concerns regarding the incomplete method step and the various components of the cosmid and DNA sequences.

Claim 9 has been amended to clarify the structure (circular DNA construct) and components (a DNA sequence and an adenovirus genome DNA) of the cosmid/adenovirus vector. The claim now specifies the components of the DNA sequence/cosmid sequence and clarifies the insertion site of the DNA sequence (i.e., the deletion site of either an E1 region or E1 and E3 regions of the adenovirus genome DNA).

Furthermore, it is noted that the E1 and E3 regions are well known in the art. In this regard, Kojima, cited in the prior art rejection, also inserts foreign genes into the deleted E1 region or E3 region of the adenoviral genome.

This amendment to claim 9 overcomes the Examiner's concerns regarding the structural elements of the vector of claims 9-11, specifically, the insertion "site" and the relationship of the cosmid and expression cassette to the E1 and E3 regions. This amendment also reflects the description at page 6, lines 16-20 of the specification which indicates that a cosmid/adenovirus vector means a circular DNA construct comprising a cosmid sequence inserted into the deletion sites of the deletion site of either the E1 region or the E1 and E3 regions of the adenovirus DNA. See also page 4, lines 6-7, 26-27, page 9, lines 8-20, Figure 1, and the Abstract.

Therefore, the rejection of claims 1-4 and 9-11 under 35 U.S.C. § 112, second paragraph, is untenable and should be withdrawn.

IV. REJECTION UNDER 35 U.S.C. § 103

Claims 1-4 and 9-11 were rejected under 35 U.S.C. § 103(a) as obvious over Kojima et al., Chen et al., and Snaith et al., cited in the PTO-1449 Forms submitted January 18, 2002 and February 22, 2002. See pages 5-6 of the Office Action.

This rejection is respectfully traversed as applied to the amended claims for the following reasons.

To establish obviousness, three criteria must be met. First, the prior art references must teach or suggest each and every element of the claimed invention. Second, there must be some suggestion or motivation in the references to either modify or combine the reference teachings to arrive at the claimed invention. Third, the prior art must provide a reasonable expectation of success.

The cited references fail to render obvious the claimed invention, because they fail to disclose or suggest each and every element of the claimed invention, namely the structural elements of the claimed vector whereby the expression cassette is inserted into the outer sequence of the DNA sequence of the vector.

The claims call for an adenovirus vector comprising an adenovirus genome DNA and a DNA sequence, wherein the DNA sequence consists of a cosmid sequence having recombinase recognition sequences at both ends and outer sequences extended from the recombinase recognition sequences, and at least one of the outer sequences has a cloning site for the insertion of the expression cassette.

The cited references fail to disclose or suggest this structural element of the claimed recombinant adenovirus vector. In fact, the adenovirus vector of the combined teachings of the cited references is structurally different from the claimed construct.

For instance, the primary reference of Kojima is relied upon for disclosing the structural components of a recombinant cosmid/adenovirus vector. However, the recombinant cosmid/adenovirus vector of Kojima, i.e., pacad1A vector, is **structurally different** from the claimed construct. In this regard, the pacad1A vector consists of the adenovirus genome DNA and the cosmid sequence. Moreover, as shown in Fig. 1 of Kojima, each end of the cosmid sequence for the pacad1A vector is connected with each end of the adenovirus DNA from which El or E3 region is deleted. Foreign genes are then inserted into the deleted El or E3 region of the adenoviral genome

is deleted. Foreign genes are then inserted into the deleted El or E3 region of the adenoviral genome DNA.

This prior art construct, as exemplified by the pacad1A vector, structurally differs from the construct of the claimed invention. In the vector construct of the claimed invention (see claim 9 for instance), the DNA sequence containing the cosmid sequence and the outer sequence is inserted into the deleted El and/or E3 regions of the adenovirus genome, and the foreign gene (expression cassette) is inserted into the outer sequence. Please compare Fig. 1 of this application and Fig. 1 of Kojima.

Another difference between the present invention and Kojima is the cleavage sites of the adenovirus genome. In Kojima, the adenovirus genome is firstly cleaved at LTR site to prepare a straight fragment. Next, the adenovirus genome DNA in pacad1A is cleaved again at the El or E3 site for the insertion of foreign gene.

This contrasts with the claimed invention wherein the adenovirus genome DNA is cleaved only one time at El and/or E3 regions for inserting the DNA sequence. Moreover, it is well understood that multiple cleavages of the viral genome diminish the virus activity, and thereby, decreasing the efficiency for obtaining the recombinant adenovirus. Thus, not only does the prior art vector of Kojima differ structurally from that of the claimed invention, but it also has different activity due to the multiple cleavage sites.

It is clear that the recombinant vector of Kojima is different from that of the claimed invention and that Kojima fails to disclose or suggest the structure of the claimed adenovirus vector.

The secondary references of Chen and Snaith also fail to disclose the structural elements of the claimed adenovirus vector. These references are relied upon for disclosing the action of different recombinases on the adenovirus genome. However, they mention nothing regarding the insertion site of the expression cassette nor the structural elements of the adenovirus vector of the claimed invention.

In view of the above, it is clear that the cited references fail to disclose or suggest each and every element of the claimed invention. As such, the cited references cannot render obvious the

claimed invention. Therefore, the rejection of claims 1-4 and 9-11 under 35 U.S.C. § 103(a) as obvious over Kojima, Chen and Snaith is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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ATTACHMENT TO AMENDMENT & REPLY:

1. Marked-up copy of Fig. 1.